RESEARCH ARTICLE

TORCH Infection and Its Influence on High-risk Pregnancy

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Abstract

Introduction: Toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex virus (TORCH) infections are important groups of organisms which are initially inapparent, asymptomatic, and difficult to diagnose on the clinical ground during pregnancy but have the potential to cause bad obstetrical outcomes. The aim was to study the association of TORCH infection with the perinatal outcome in cases of high-risk pregnancies.

Materials and methods: A total of 200 high-risk pregnant patients of age group <35 years attending Antenatal Care Outpatient Department or admitted in Inpatient Department of Obstetrics and Gynaecology Department at Acharya Vinoba Bhave Rural Hospital, Sawangi, were included in the present study. The study group includes high-risk pregnant women with fetal congenital anomalies, recurrent pregnancy loss, oligohydramnios, intrauterine fetal death, fetal growth restriction, hypertensive disorders, bad obstetric history, preterm labor, polyhydramnios, and other medical disorders. Patient's serum was analyzed for IgG (immunoglobulin G) and IgM (immunoglobulin M) antibodies against TORCH agents using ELISA kit and followed till delivery for the perinatal outcome. Perinatal outcome in high-risk pregnant women with seropositivity and seronegativity was compared.

Results: In 200 cases of high-risk pregnancy, the majority of women with seropositivity for TORCH infection were of younger age group with low parity, residing over rural areas and of low socioeconomic status. One hundred sixty-two cases (81%) were seropositive and 38 cases (19%) were seronegative for TORCH antibodies. The seropositivity in high-risk pregnant women for toxoplasma, rubella, cytomegalovirus, and herpes was 5.5, 75.5, 56, and 14.5%, respectively for IgG, while it was 0, 6, 4, and 0% for IgM, respectively. Our study showed that pregnant patients with high-risk factors for TORCH infection with seropositivity showed a significant association with adverse perinatal outcomes.

Conclusion: Association of seropositivity with high-risk factors for TORCH infection was found to be associated with adverse perinatal outcome as compared to seronegativity in same high-risk groups.

Keywords: High-risk pregnancy, Perinatal outcome, Seronegativity, Seropositivity, TORCH.

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Introduction

For thousands of couples, the joyous event of birth of a child in their family may become the beginning of a long tortuous and tumultuous life. Human reproduction is a relatively insufficient process.[1] Pregnancy loss is a challenging and frustrating problem for couples and clinicians alike. Miscarriage is often associated with guilt, embarrassment, and depressive states.[2]

"High-risk pregnancy (HRP) is a condition where the mother or the developing fetus or both are at an increased risk for complications during or after pregnancy and at birth."[3] Bad obstetric outcome is a multifactorial condition, in which one of the major causes is maternal infection. One of the maternal infections caused by toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex virus (TORCH) group of organisms usually goes unnoticed and undiagnosed, which is transmitted in utero at several stages of pregnancy and causes adverse perinatal outcomes.

The TORCH infections are important groups of organisms which are initially inapparent, asymptomatic, and difficult to diagnose on the clinical ground during pregnancy but have the potential to cause bad obstetrical outcome in the form of congenital anomalies, oligohydramnios, FGR (fetal growth restriction), IUFD (Intrauterine fetal death), recurrent pregnancy loss (RPL), and stillbirth. The acronym TORCH was coined by immunologist Andre Nahmias.[1] TORCH is an acronym which stands for toxoplasmosis, other agents, rubella, cytomegalovirus (CMV), and herpes simplex virus (HSV) infection. The majority of TORCH infections cause mild maternal illness, but the fetal consequences are serious. Treatment of maternal infection frequently has no impact on fetal outcomes. Early recognition of maternal disease and fetal monitoring once the disease is recognized are vital. Knowledge of these diseases can help the clinician appropriately counsel mothers on preventive measures to avoid these infections and aid in counseling parents on the potential for adverse fetal outcomes when these infections are present.[4]

Toxoplasmosis in human beings is caused by *Toxoplasma gondii*, an intracellular protozoan parasite, that is transmitted through contaminated food or water and undercooked meat. The incubation period is 5–23 days after ingesting the cysts. The infected women are usually asymptomatic, and during pregnancy, they may undergo pregnancy loss, stillbirth, and intrauterine malformations in the fetus.[5,6]

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Rubella infection is transmitted from person to person by tiny droplets in air and mother to child through placental transfer. This disease lasts for 1–5 days and the incubation period is 2–3 weeks.[7] It usually presents as a mild or asymptomatic infection in children and adults. However, the virus may cross the placenta and could result in miscarriage, fetal death, or an infant with serious birth defects including hearing impairment, cataracts, and cardiac defects, collectively known as congenital rubella syndrome.[8]

CMV is ubiquitous and species specific. Human beings are the reservoir hosts for this virus and the viruses are transmitted by direct contact with saliva, urine, and genital secretions. In pregnant women, the transmission is by direct contact with infected urine or saliva from young children or through sexual activity.[9] The incubation period of CMV infection ranges between 4 and 12 weeks. In neonates, the symptoms include intrauterine growth retardation, microcephaly with intracranial calcification, hepatosplenomegaly, jaundice, chorioretinitis, thrombocytopenic purpura, and anemia.[10] The major childhood disabilities like loss of vision, hearing, and cognitive impairment are also due to CMV infection.[11]

HSV is the most common sexually transmitted viral disease worldwide. HSV1 is transmitted during childhood by nonsexual contacts, while HSV2 is always transmitted sexually and is the major cause of genital herpes.[12,13] Incubation period of herpes ranges between 4 and 21 days. In more than 75% of cases, primary genital HSV infection remains asymptomatic.[14] In newborns, this infection remains a major cause of morbidity and mortality.[15–17] Genital herpes infection during pregnancy may lead to spontaneous abortion, prematurity, or congenital and neonatal herpes.[17,18]

Most of the maternal infections are initially asymptomatic. Diagnosis based on the clinical presentation is difficult. Thus, the diagnosis of these infections largely depends on serological evidence.[1] Utilizing TORCH panel for screening may help prevent many of these potential birth defects, as some of the TORCH infections can be effectively treated if the mother is diagnosed early in her pregnancy. Detection of IgM antibody against toxoplasma, rubella, HSV, and CMV is the best diagnostic modality for these infections. A national screening program for TORCH infections is lacking in INDIA. There are some controversial studies about the association between TORCH infection and adverse perinatal outcomes. Hence, we have decided to study the association between various HRPs and the relationship with perinatal outcome.

Materials and Methods

Institute's ethical committee approval was taken and, after explaining in detail the methodology of the study, an informed valid written consent was obtained from all the eligible subjects.

Sample Size

At 95% confidence level,

Expected proportion taken as 50%

Absolute error or precision 7.5%

$n = Z_{1-\alpha/Z}{}^2\, P(I - P)/\delta^2$

n = sample size, $Z_{1-\alpha} = 1.96$, value of standard normal variable corresponding to the level of significance alpha 5%, P = expected proportion, $q = I - P$, δ = absolute error or precision, $n = 1.96^2 \times 50\ (100 - 50)/7.5^2$

Minimum sample size = 171 (rounded up to 200, which is adequate for the study)

In the present observational study, a total of about 200 pregnant patients of age group <35 years attending Antenatal Outpatient Department or admitted in Inpatient Department of Obstetrics and Gynaecology, Department at Acharya Vinoba Bhave Rural Hospital, Sawangi, during 2 years (2017–2019) were selected and included in the present study. The pregnant women with fetal congenital anomalies, oligohydramnios, IUFD, FGR, hypertensive disorders, preterm labor, polyhydramnios, and other medical disorders (like thyroid dysfunction, diabetes mellitus, heart diseases, sickle cell hemoglobinopathy, and anemia) in present pregnancy and pregnant patients with RPL and BOH (bad obstetric history) were included, while pregnant patients of age >35 years with consanguineous marriage and fetal congenital malformations caused due to exposure to teratogenic drugs, noxious gases, etc., were excluded.

Patients were evaluated on the basis of predesigned pro forma with respect to history, clinical examination, and investigation. Two milliliters of blood obtained aseptically from each woman in a duly labeled plain test tube was kept at room temperature for 20 minutes. The sample was then centrifuged and sera were separated and stored at –20°C until tested. Serum was analyzed for IgG (immunoglobulin G) and IgM (immunoglobulin M) antibodies against TORCH agents using a commercially available ELISA kit (Calbiotech, El Cajon, CA, USA] following the manufacturer's instruction. The optical density (OD) at 450 nm with a filter of 600 to 650 nm dual-wavelength mode was measured by microwell ELISA reader (Robonik Elisa Plate Analyzer). The intensity of color generated was proportional to the amount of specific antibody in the sample. Negative and positive controls were used provided in the kit. The results were interpreted by immune status ratio index, calculated by dividing the specimen OD value by the cutoff calibrator ratio (calibrator OD × calibrator factor) in the central research laboratory of Jawaharlal Nehru Medical College of Datta Meghe Institute of Medical Sciences, Sawangi. ELISA kits used were having sensitivity >98% and specificity >98%. Results of seropositivity and seronegativity for TORCH infections were recorded by levels of IgG and IgM in antenatal patients. These readings were standardized and followed by Federation of Obstetric & Gynecological Societies of India guidelines.[19] The statistical analysis was drawn on the basis of results obtained using Chi-square test and calculating odds ratio (OR) at 95% confidence interval for risk analysis. Software used is SPSS version 21.0. P-value < 0.05 and OR >2 were considered significant.

Antibody index interpretation: [As per criteria given in ELISA kits from Calbiotech, El Cajon, CA, USA] <0.9—no detectable antibody, 0.9–1.1—borderline positive, >1.1—detectable antibody. Patients showing seropositivity and seronegativity were followed till delivery for the perinatal outcome. Thereafter, the outcome of seropositivity and seronegativity in high-risk pregnant women was compared.

Results

A total of 200 high-risk pregnant women were studied for a period of 2 years. As displayed in Table 1, it was observed that the majority of high-risk pregnant women with seropositivity for TORCH infection were of younger age group with low parity, residing over rural areas and of low socioeconomic status. In 200 cases of HRP, 162 cases (81%) were seropositive and 38 cases (19%) were seronegative for TORCH antibodies, as shown in Figure 1.

Figure 2 depicts that seropositivity for toxoplasma IgG antibody was 5.5%, while no patients in the study group had IgM positive for toxoplasma. For rubella IgG, 75.5% of pregnant women showed

Table 1: Distribution of demographic characteristics in high-risk pregnant women [200]

Variable	*No. of cases*	*Percentage (%)*
Maternal age		
<25 years	103	51.5
26–29 years	77	38.5
>30 years	20	10
Gravida		
1	77	38.5
2	56	28
3 or more	67	33.5
Religion		
Hindu	193	96.5
Muslim	7	3.5
Others	0	0
Residence		
Rural	186	93
Urban	14	7
Maternal education		
Middle school or less	132	66
High and higher secondary	56	28
Graduate and more	12	6
Maternal occupation		
Housewife	79	39.5
Laborer	65	32.5
Skilled workers	45	22.5
Professionals	11	5.5
Family income		
<5,000	48	24.0
5,000–10,000	125	62.5
>10,000	27	13.5
***Socioeconomic status**		
Upper (I)	1	0.5
Upper middle (II)	1	0.5
Middle (III)	10	5
Lower middle (IV)	20	10
Lower (V)	168	84

*According to modified B.G. Prasad scale 2017, socioeconomic status is divided into five groups

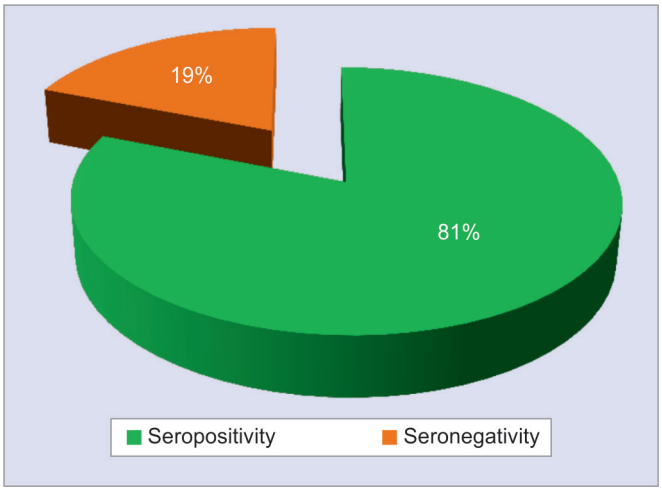

Fig. 1: Percentage of cases according to seropositivity and seronegativity for TORCH infection in the study group

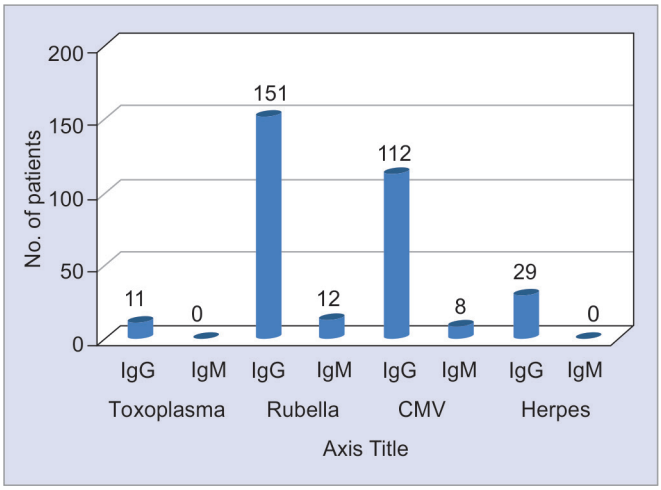

Fig. 2: Seropositivity for TORCH infection in high-risk cases (162 cases)

seropositivity, while 6% were positive for IgM anti-rubella antibody. The seropositivity of pregnant women for CMV IgG and IgM was 56 and 4%, respectively. With respect to HSV, 14.5% of pregnant women were positive for IgG and none of them were positive for IgM antibodies.

**p*-value <0.05 ***p*-value <0.001

In our study of 200 high-risk pregnant women, maximum risk factors were hypertensive disorder in 41 patients (20.5%), then oligohydramnios in 38 (19%) patients, and 24 patients (12%) with congenital anomaly while preterm labor in 19 patients (9.5%), eighteen cases of FGR (9%), fifteen cases of RPL (7.5%) present, twelve cases of polyhydramnios (6%), eleven cases of previous BOH (5.5%), and eight cases of IUFD (4%).

Table 2 depicts the correlation of high-risk factors in present pregnancy with seropositivity for TORCH agents.

Eight different perinatal outcomes were found in different high-risk factors in pregnant patients as shown in Table 3.

- Premature baby (25 cases)—92% premature babies were the outcome of seropositive cases, while 8% were of seronegative cases of HRP.
  Rubella IgG and CMV IgG are maximum seropositivity present. There is a highly significant association of preterm labor as a risk factor with premature baby (*p*-value <0.001) with a very high OR (30.514). Significant association was seen between oligohydramnios and premature baby (*p*-value <0.05).
- Dead baby (eight cases)—87.5% dead babies were the outcome of seropositive cases, while 12.5% were of seronegative cases of HRP. Dead baby has a significant association with toxoplasma IgG (*p*-value <0.05). Toxoplasma IgG is a risk factor for dead babies (OR 6.778).
- Anomalous baby (24 cases)—91.7% anomalous baby were the outcome of seropositive cases, while 8.3% were of seronegative cases of HRP.
  A very high significant association was present with congenital anomaly (*p*-value 0.000). Significant association was present between anomalous baby with CMV IgM, rubella IgM, and toxoplasma IgG (*p*-value <0.05).
- Abortus (three cases)—100% abortus were the outcome of seropositive cases. Nil cases were seronegative.

Table 2: Correlation of high-risk factors in present pregnancy with seropositivity for TORCH agents

	Toxoplasma		*Rubella*		*Cytomegalovirus*		*Herpes*	
Risk factors	*IgG (%)*	*IgM (%)*	*IgG (%)*	*IgM (%)*	*IgG (%)*	*IgM (%)*	*IgG (%)*	*IgM (%)*
Preterm labor (19)	0	0	17	0	9	0	4	0
	0	0	11.3	0	8.0	0	14.3	0
Intrauterine fetal death (8)	1*	0	5	3*	5	0	2	0
	9.1	0	3.3	25	4.5	0	7.2	0
Fetal growth restriction (18)	0	0	16	0	13	0	4	0
	0	0	10.6	0	11.6	0	14.3	0
Oligohydramnios (38)	0	0	25	0	19	0	2	0
	0	0	16.6	0	17.0	0	7.1	0
Previous bad obstetric history (11)	0	0	11	1	8	1*	0	0
	0	0	7.3	8.3	7.1	12.5	0	0
Congenital anomaly (24)	4*	0	21	6**	15	6**	3	0
	36.4	0	13.9	50.0	13.4	75.0	10.7	0
Hypertensive disorder (41)	2	0	32	1	24	0	9	0
	18.2	0	21.2	8.3	21.4	0	32.2	0
Polyhydramnios (12)	1	0	10	0	10	0	5	0
	9.1	0	6.6	0	8.9	0	17.9	0
Recurrent pregnancy loss (15)	0	0	13	0	12	0	0	0
	0	0	8.6	0	10.7	0	0	0
Other medical disorders (18)	2	0	11	1	10	1	3	0
	18.2	0	7.3	8.3	8.9	12.5	10.7	0
Total (200)								

*p-value <0.05, **p-value <0

Significant association was also present between abortion and CMV IgM (p-value <0.05). CMV IgM is a risk factor for abortion (OR 13.571).

There is a high risk of abortion with BOH (OR 9.350). There is a significant association of BOH with abortion (p-value <0.05).

- Stillbirth (three cases)—100% stillbirths were outcome of seropositive cases. Nil cases were seronegative.

  Rubella IgM and herpes IgG are risks associated with stillbirth as perinatal outcome (OR >2).
- Early neonatal death (six cases)—100% early neonatal deaths were outcome of seropositive cases. Nil cases were seronegative.

  In our study, CMV IgM is a strong risk factor for early neonatal death (OR 5.343).

  Significant association was seen between early neonatal death and preterm labor as a risk factor (p-value <0.05, OR 5.206).
- Neonatal intensive care unit (NICU) admission (18 cases)—100% early neonatal deaths were outcome of seropositive cases. Nil cases were seronegative.

  NICU admission has a significant association with rubella IgM (p-value <0.05). FGR as a risk factor is significantly associated with NICU admission of the newborn (p-value <0.05).
- Normal baby (115 cases)—among seropositive cases, 51.2% were normal babies, while among seronegative cases, 84.2% cases had normal babies.

  Significant association was present between seronegativity and normal baby (p-value <0.05).

  High-risk patients are seropositive for TORCH infections in the majority of the cases.

  Thus, it is clear that seronegative cases have a more normal outcome than seropositive cases of HRP.

Discussion

In our study, the maximum number of patients were in the age group of less than 25 years (51.5%) as shown in Table 1. This may be because maximum patients were of rural areas in our study. Rubella shows maximum seropositivity among all age groups followed by CMV. This is comparable with the study done by Rebekah et al.[20] In our study, the maximum of our study population was from rural areas (83%) and studied till middle school (34.5%). The maximum number of patients was housewives and laborers in our study (72%). Maximum seropositive cases were from the lower class (168 cases, 84%). In the lower class, the number of cases was maximum for anti-rubella IgG antibody (84.8%) followed by CMV IgG (83.9%). Study done by Turbadkar et al.[21] and Rajani[4] is comparable with our study. In our study, we observed high-risk patients were more common in primigravida patients (38.5%), which was comparable to a study done by Rebekah et al.[20]

Seropositivity for Torch Infection

In our study of 200 cases, 162 cases (81%) were seropositive and 38 cases (19%) were seronegative for TORCH antibodies.

The seropositivity for toxoplasma IgG antibody was 5.5%, while no patients had IgM positivity for toxoplasma. Pregnant women of 75.5% showed seropositivity for rubella IgG antibody, while 6% were positive for IgM anti-rubella antibody. The seropositivity of pregnant women for CMV IgG and IgM was 56 and 4%, respectively. With respect to HSV, 14.5% were positive for IgG and nil for IgM antibodies.

The studies done by Kumar et al.,[1] Pradhan,[22] Padmavathy et al.,[23] and Tatjana et al.[24] were comparable with our study for seropositivity for TORCH infections.

Perinatal Outcome

1. Perinatal outcome with seropositivity for TORCH infection:

   In our study of total 200 cases, 8 different perinatal outcomes were found. There were dead baby (4%), NICU admission (8%), anomalous baby (12%), abortion (1.5%), early neonatal death (3%), stillbirth (1.5%), prematurity (12.5%), and normal baby (57.5%).

   - Dead baby has significant association with toxoplasma IgG (p-value <0.05). Also, toxoplasma IgG is a risk factor for IUFD (OR 6.778).
   - NICU admission has significant association with rubella IgM (p-value <0.05).
   - Rubella IgG is a risk factor for NICU admission (OR 2.477).
   - There is a strong association between CMV IgM antibody and anomalous baby (p-value <0.001). CMV IgM is a very

Table 3: Association of perinatal outcome with TORCH infection in high-risk pregnancy

S. No.	Perinatal outcome (total)		Toxoplasma IgG	Toxoplasma IgM	Rubella IgG	Rubella IgM	Cytomegalovirus IgG	Cytomegalovirus IgM	Herpes IgG	Herpes IgM	Seronegative cases
1	Dead baby (8)	Cases	2	0	5	3	5	0	2	0	1
		P-value	0.014	–	0.383	0.589	0.758	0.556	0.360	–	0.966
		OR	6.778	–	0.525	1.495	0.795	1.43	2.128	–	0.954
2	Neonatal intensive care unit admission (18)	Cases	0	0	14	1	11	0	3	0	0
		P-value	0.314	–	0.245	0.008	0.911	0.395	0.568	–	0.107
		OR	1.064	–	2.401	1.460	1.065	–	1.468	–	1.165
3	Anomalous baby (24)	Cases	4	0	21	6	15	6	3	0	2
		P-value	0.011	–	0.145	0.645	0.577	0.000	0.821	–	0.469
		OR	4.829	–	2.477	0.795	0.778	29.000	0.863	–	0.576
4	Abortus (3)	Cases	0	0	2	1	2	1	0	0	0
		P-value	0.674	–	0.720	0.868	0.975	0.009	0.481	–	0.500
		OR	–	–	0.644	1.228	0.962	13.571	–	–	1.152
5	Early neonatal death (6)	Cases	0	0	6	1	4	1	1	0	0
		P-value	0.549	–	0.157	0.499	0.965	0.108	0.848	–	0.336
		OR	–	–	1.338	0.481	0.962	5.343	1.237	–	1.155
6	Stillbirth (3)	Cases	0	0	2	2	2	0	1	0	0
		P-value	0.674	–	0.720	0.147	0.975	0.722	0.331	–	0.500
		OR	1.059	–	0.644	5.036	0.962	1.042	3.148	–	1.152
7	Premature baby (25)	Cases	0	0	22	6	16	0	3	0	2
		P-value	0.197	–	0.120	0.556	0.690	0.275	0.758	–	0.427
		OR	1.067	–	2.615	0.747	0.837	–	0.818	–	0.547
8	Normal baby (113)	Cases	5	0	81	0	81	0	15	0	32
		P-value	0.366	–	0.014	0.109	0.535	11.747	0.326	–	0.013
		OR	0.573	–	0.418	1.684	1.208	–	0.792	–	3.413
	Total (200)										

high risk factor for anomalous baby as perinatal outcome (OR 29.00).

- Significant association is also present between anomalous baby and toxoplasma IgG (*p*-value <0.05), with toxoplasma IgG also as a risk factor for anomalous baby (OR 4.829).
- Significant association is also present between abortion and CMV IgM (*p*-value <0.05). CMV IgM is a risk factor for abortion (OR 13.571).
- In our study, CMV IgM is also a strong risk factor for early neonatal death (OR 5.343).
- Rubella IgM and herpes IgG are risks associated with stillbirth as perinatal outcome (OR >2).
- Rubella IgG is a risk associated with prematurity as perinatal outcome (OR >2).

The above-mentioned points show the significance of seropositivity for TORCH agents with a poor perinatal outcome. In our study, we have only studied the association of seropositivity and perinatal outcome in HRP.

In the study done by Kumar et al.,[1] of 75 women with HRP, 40 (53.33%) had RPL, 16 (21.33%) had IUFDs, 6 (8%) had early neonatal deaths, and 4 (5.33%) had congenital malformations. Another study done by Sarkar et al.[25] reported that 38, 9, 5, and 20% of cases of abortions, IUFDs, stillbirth, congenital malformations, and early neonatal deaths, respectively.

In study by Mohammad and Salman,[26] perinatal outcome showed a high frequency of stillbirths (94.11%), IUFD (80%), abortion (70%), and congenital malformation (63%).

2. Perinatal outcome with seropositivity for TORCH infection in different high-risk pregnant patients (Table 2).

- Preterm labor (19 patients)
  Maximum seropositivity in preterm patients was found as rubella IgG (84.21).
  Perinatal outcome among them was maximum as a premature baby (13 cases, 68.4%).
  There was a highly significant association of preterm labor as a risk factor with a premature baby (*p*-value <0.001) with very high OR (30.514). Significant association was seen between early neonatal death and preterm labor as a risk factor (*p*-value 0.043, OR 5.206).

In study done by Rebekah et al.,[20] preterm labor showed the highest seropositivity for toxoplasma (55%).

- IUFD (8 patients)
  Serologically, five patients were positive for rubella IgG and CMV IgG, three for rubella IgM, two for herpes IgG, and one for toxoplasma IgG. Significant association was found between toxoplasma IgG and dead baby as a perinatal outcome (*p*-value <0.05).
  Perinatal outcome associated with this was dead baby (eight cases, 100%). A very high significant association was present (*p*-value 0.000).

In study done by Rebekah et al.,[20] IUFD showed high seropositivity for toxoplasma (45%) and CMV (96%). This was comparable with our study.

- Congenital anomaly (24 patients)
  Serologically, 21 patients were positive for rubella IgG and 15 for CMV IgG. Six patients were seropositive for rubella IgM and CMV IgM, four for toxoplasma IgG, and three for herpes IgG. A very high significant association was found between CMV antibody IgM and rubella IgM with anomalous baby (p-value <0.001). Significant association was seen in toxoplasma IgG and anomalous baby as a perinatal outcome (p-value <0.05). There is also a higher risk of abortion associated with congenital anomaly (OR 3.783). Perinatal outcome associated with this was anomalous baby (24 cases, 100%). A very high significant association was present (p-value 0.000).

In study done by Rebekah et al.,[20] anomalous malformation showed high seropositivity for rubella (97%) and CMV (97%). This is comparable to our study.
In our study, congenital anomaly includes anencephaly, tetralogy of Fallot, ventricular septal defects, encephalocele, meningomyelocele, hydranencephaly, musculoskeletal dysplasia, congenital diaphragmatic hernia, and mesenteric cyst. Consanguinity and history of exposure to teratogenic agents were excluded from our study. However, chromosomal studies could not be done as many of the patients could not come for follow-up.

- Hypertensive disorders (41 patients)
  In patients with hypertensive disorders, the presence of rubella IgM antibody has significant association with stillbirth in our study (p-value <0.05).
  Significant association was seen between hypertensive disorders as a risk factor and normal baby delivered (p-value 0.013).
  Perinatal outcome among them was maximum for normal baby (31 cases, 75.60%). Four cases (9.75%) were NICU admissions. There were three premature babies delivered (7.31%). Early neonatal death (two cases, 4.8%) and stillbirth (two cases, 4.8%) were perinatal outcomes associated.

- Previous BOH (11 patients)
  In our study, there is a significant association between CMV IgM antibody with early neonatal death and rubella IgM with premature baby as a perinatal outcome (p-value <0.05).
  Perinatal outcome among them was maximum for normal baby (six cases, 54.54%). Two cases (18.18%) were premature babies. There was one case each of abortion, NICU admission, and early neonatal death as a perinatal outcome (9.09%).
  There is a high risk of abortion with previous BOH (OR 9.350). There is a significant association of previous BOH with abortion (p-value <0.05) in our study.

However, study done by Surpam et al.[27] in 225 patients, 150 previous BOH cases consisted of abortion in 44 (29.33%), IUGR in 32 (21.33%) cases, IUFD in 17 (11.33%) cases, premature in 11 (7.33%), early neonatal death in 25 (16.66%), and congenital malformation in 21 (14%).

- Oligohydramnios (38 patients)
  Serologically, 25 cases were positive for rubella IgG and 19 cases were positive for CMV IgG.

Perinatal outcome with oligohydramnios was maximum for normal baby (33 cases, 86.84%). Two cases had NICU admissions (5.26%). There was one case each of stillbirth, premature baby, and early neonatal death as perinatal outcome (2.63%).

Significant association was seen between oligohydramnios and premature baby as a perinatal outcome (p-value <0.05). Highly significant association was noted between oligohydramnios and normal baby (p-value <0.001).

- FGR (18 patients)
  Maximum seropositivity in FGR was seen for rubella IgG (16 cases) and CMV IgG (13 cases).
  Perinatal outcome among them was maximum for normal baby (10 cases, 55.55%). Four cases (22.22%) were NICU admissions. There were three cases of premature baby (16.66%) and one case of stillbirth (5.55%).
  FGR as a risk factor is significantly associated with NICU admission of the newborn (p-value <0.05). FGR is also a high-risk factor for stillbirth and NICU admissions (OR >2).

- Polyhydramnios (12 patients).
  Serologically, 10, 10, and 5 cases were positive for rubella IgG, CMV IgG, and herpes IgG, respectively.
  However, perinatal outcome associated with this was normal baby (12 cases, 100%). Significant association was seen between polyhydramnios and normal baby (p-value <0.05).

- RPL (15 patients)
  In our study, maximum seropositivity for RPL is seen in rubella IgG and CMV IgG.
  Perinatal outcome among them was maximum for normal baby (10 cases, 66.66%). Three cases (20%) were premature baby and two cases were NICU admissions (13.33%).

However, there is an increased risk of NICU admissions with RPL (OR 3.308).
In study done by Rebekah et al.,[20] RPL had high seropositivity for rubella (87%). This is comparable with our study.
However, other causes like uterine anomaly, incompetent os, etc.. are not elicited in our study.

- Other medical disorders (18 patients)
  Other medical disorders included thyroid dysfunction, diabetes mellitus, heart diseases, sickle cell hemoglobinopathy, and anemia.
  In our study, maximum seropositivity for other medical disorders is seen in rubella IgG followed by CMV IgG.
  Also, there is increased risk of abortion with other medical disorders (OR 5.294).
  There was a significant association between other medical disorders and normal baby (p-value <0.05).
  Perinatal outcome among them was maximum for normal baby (16 cases, 88.88%). There was one case each of abortion and NICU admissions (5.55%).

3. Perinatal outcome with seronegativity for TORCH infection in different high-risk pregnant patients.
   Of 38 seronegative cases, 32 (84.2%) had normal baby as outcome, which is significantly associated (p-value <0.05).
   Maximum seronegative cases were seen with oligohydramnios as a risk factor.

Conclusion

From our study, we conclude that association of seropositivity for TORCH infection with high-risk factors was found to be associated with adverse perinatal outcome as compared to seronegativity in same high-risk groups. As it is not made a

protocol for screening of high-risk cases for TORCH, it should be considered for high-risk cases for diagnosis and management to get better perinatal outcome. Screening and early diagnosis of TORCH infection in high-risk patients have a definite role in early detection and appropriate management to prevent perinatal morbidity and mortality. Neonatal screening of congenital TORCH infection could not be carried out due to the nonavailability of facilities. Follow-up after 1 month was found difficult in IgM-positive cases due to noncompliance of patients from rural areas. Chromosomal study could not be carried out in patients with congenital anomalies as there were many defaulters in this group for further follow-up.

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